DUX4 overexpression in proliferating myoblasts induces an early response of the metabolic sensor AMPK

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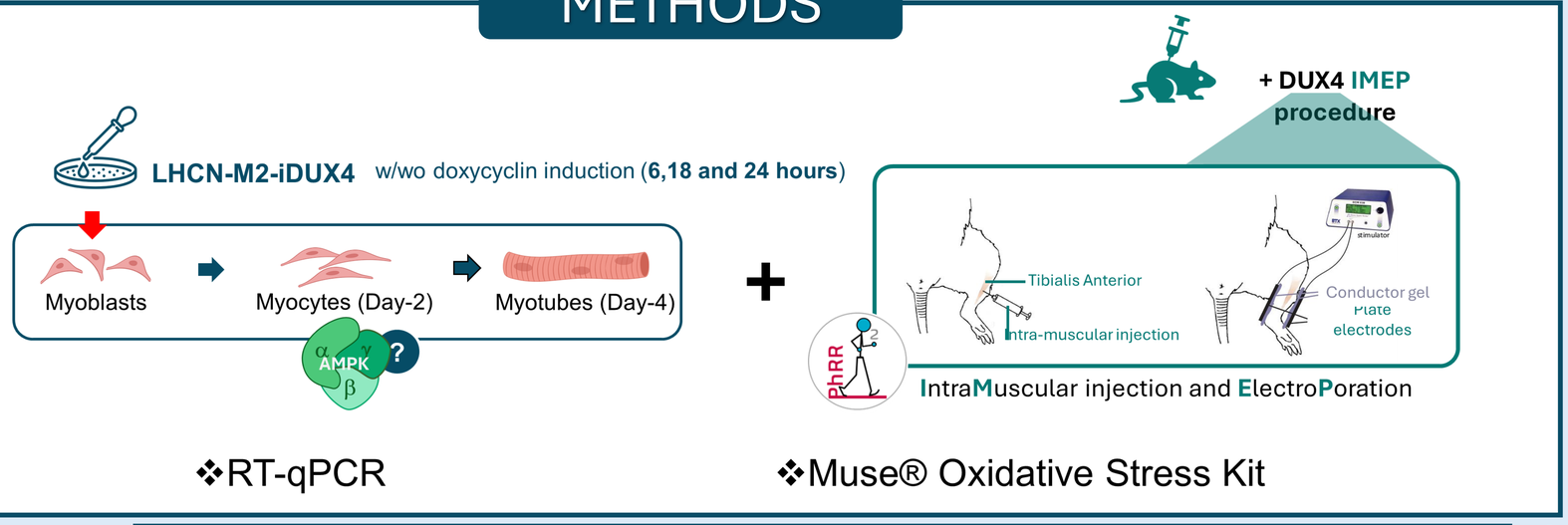
INTRODUCTION

Recent studies highlight metabolic stress and mitochondrial dysfunction as key features of FSHD muscle pathology induced by DUX4 expression. Among the affected regulators, a reduction in *PPARGC1A* which encodes the mitochondrial biogenesis coactivator PGC-1α has been reported in FSHD muscle cells. Since PGC-1α activity depends on AMPK-mediated phosphorylation and given the beneficial role of AMPK in various myopathies, we investigated the early impact of DUX4 expression on the AMPK–PGC-1α axis *in vitro* and *in vivo.*

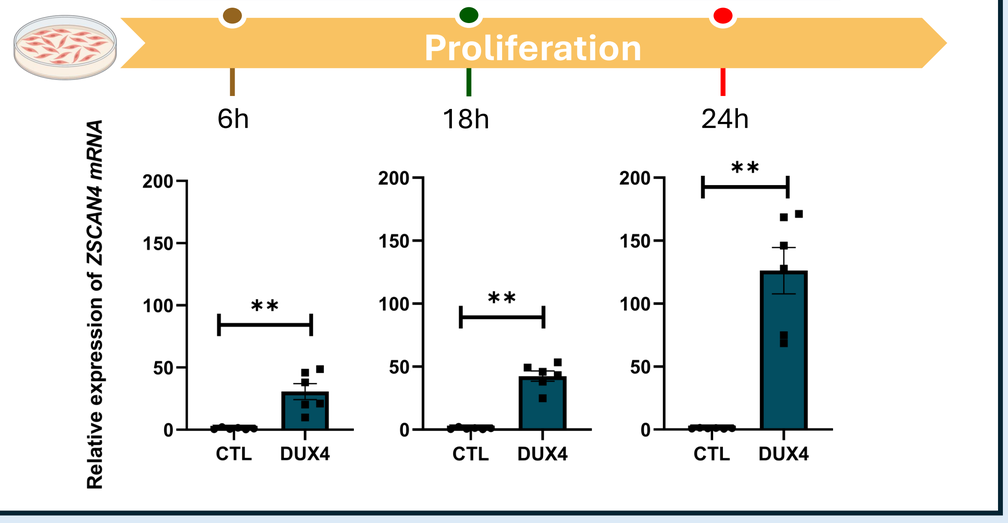
AIM

To explore the early impact of DUX4 overexpression on mitochondrial regulation by investigating the AMPK–PGC-1α axis in LHCN-M2-iDUX4 myoblasts, in the context of FSHD-associated metabolic stress.

METHODS

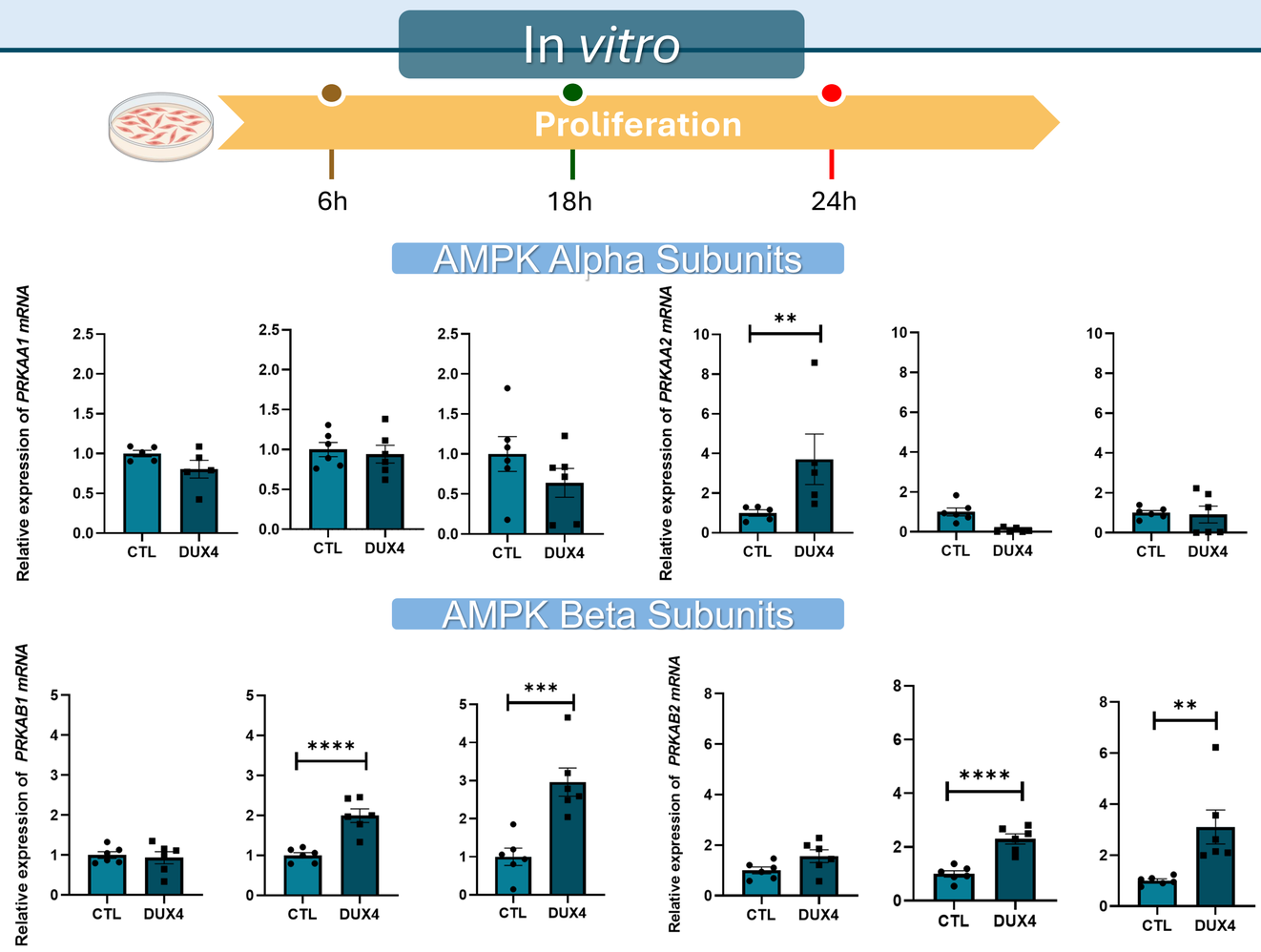


Model Validation

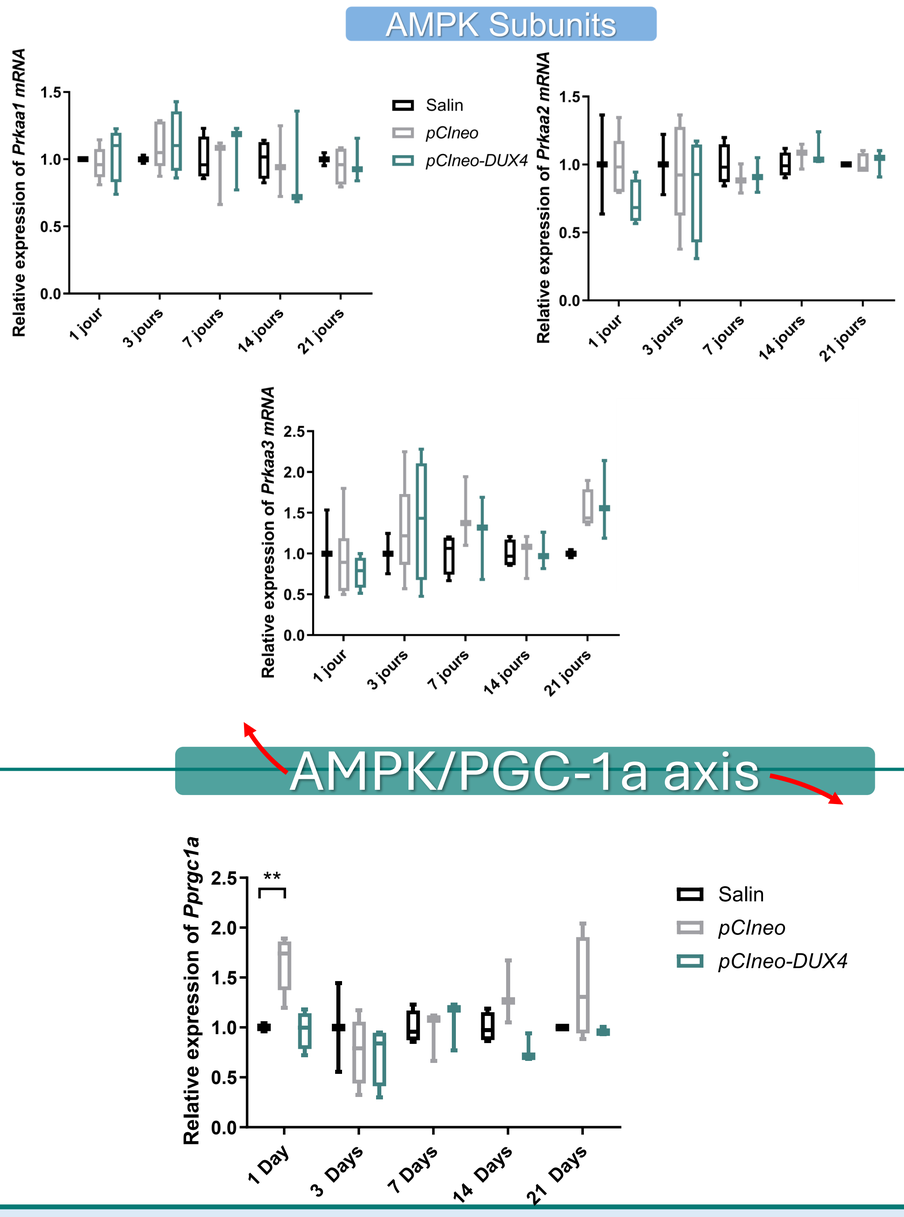


RESULTS

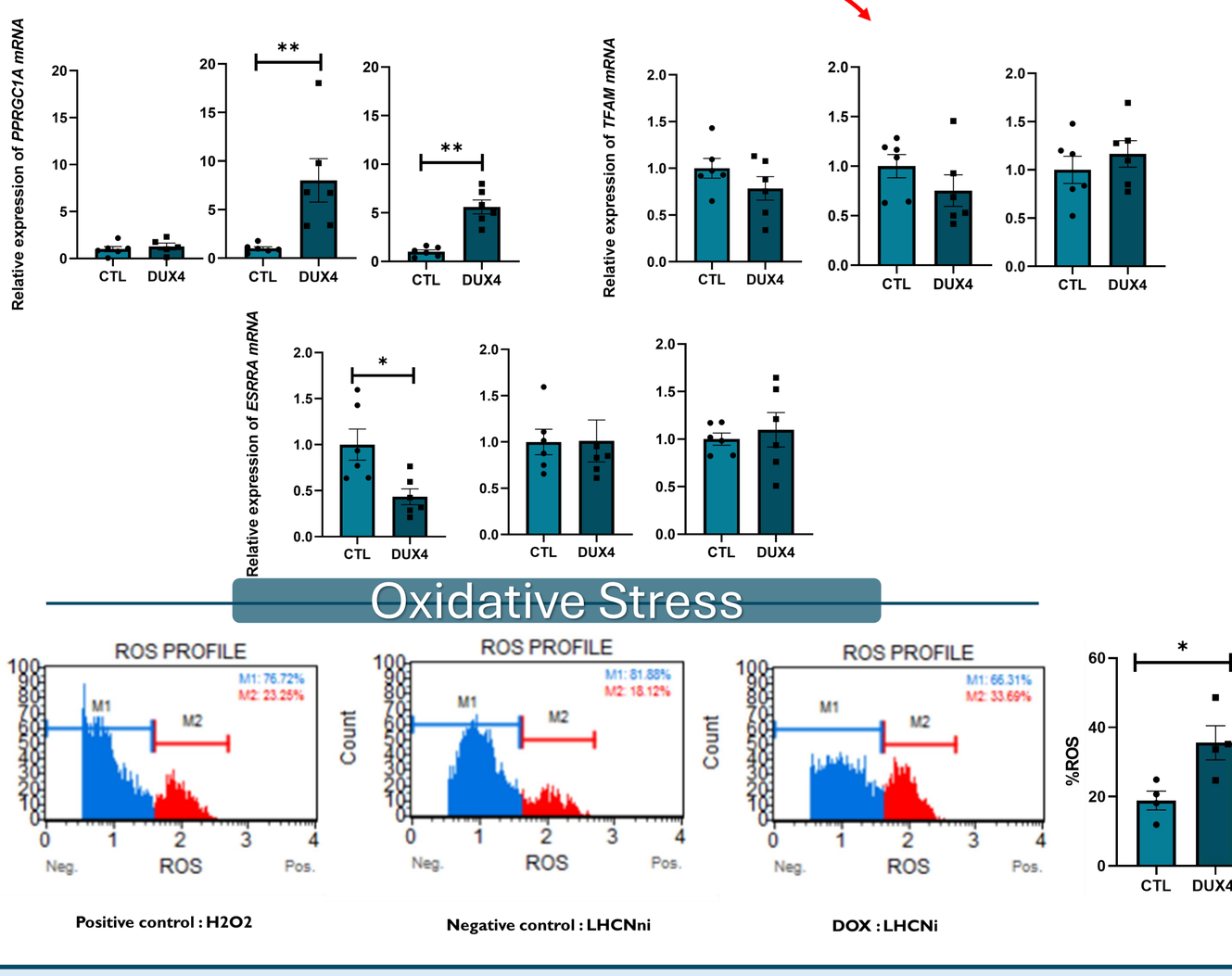
In *vitro*



In *vivo*



AMPK/PGC-1a axis



Oxidative Stress

TAKE-HOME MESSAGES

Our results reveal an upregulation of *PPARGC1A* and *AMPK* subunits in response to early DUX4 induction in myoblasts, suggesting a potential compensatory mechanism to counteract mitochondrial dysfunction. Further investigations are needed to clarify the functional significance of these changes in the context of FSHD.

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